REMARKS

Claims 1 and 2 have been amended to specify that "mouse" is a transgenic mouse. Claims 3 and 4 have been amended to specify "isolated" mouse cells. Claims 5, 9 and 10 have been amended to indicate the term for "SVAS" and to clarify the language of the claims with respect to the ELN +/- mouse, ELN +/- human, ELN +/- mouse cells or ELN +/-human cells. It is submitted that these amendments do not constitute new matter, and their entry is requested.

The Examiner rejected claims 1-4 under 35 U.S.C. §101 as being directed to non-statutory subject matter. Applicants do not agree with the Examiner's contention that the claims read on naturally-occurring mice or mouse cells which meet the limitations of the claims, and note that the Examiner has cited no reference in support of this contention. Nevertheless, in an effort to advance prosecution of this application, Applicants have amended the claims as suggested by the Examiner. Withdrawal of this rejection is requested.

The Examiner rejected claims 5, 9 and 10 under 35 U.S.C. §112, second paragraph, for being indefinite. It is believed that the amendment of these claims to clarify the language with respect to the ELN +/- mouse, ELN +/- human, ELN +/- mouse cells or ELN +/-human cells obviates this rejection. Withdrawal of this rejection is requested.

The Examiner rejected claims 3-4 under 35 U.S.C. §103 as being unpatentable over Keating (*Cardiovasc Res* 36:134-137, 1997) in view of Wydner et al. (*Genomics* 23:125-131, 1994). It is submitted that the Examiner is in error in this rejection.

In making this rejection, the Examiner argues that Keating teaches that SVAS is a component of William's syndrome which is associated with deletion of one elastin allele, and further suggests breeding mice with a targeted knockout elastin gene to determine clinical consequences of the animal model. Wydner et al. is cited to show the cDNA sequence for the mouse elastin gene. The Examiner concludes that it would have been obvious to use the known cDNA sequence of the mouse elastin gene to generate a mouse lacking one or both elastin gene because Keating teaches deletion of one elastin gene in WS and suggests making a mouse model having a knocked-out elastin gene. Such a mouse lacking one or both elastin genes would have

mouse cells comprising only one functional elastin gene, or no functional elastin gene, in its genome.

Although the Examiner is correct in that Keating suggests making a mouse knockout model, the gene that Keating teaches should be knocked out is not the elastin gene. Instead, it is the "candidate gene" which may be contiguous to the elastin gene, and which is also deleted in William's syndrome and may be responsible for the features other than SVAS in William's syndrome. Thus, Keating suggests knockouts with this candidate gene and not with the elastin gene. Consequently, there is no suggestion or motivation in Keating et al. to knock out the elastin gene. Nor is there any suggestion or motivation in Wydner et al. to prepare a knockout mouse in which the elastin gene is knocked out, even though Wydner et al. shows the cDNA sequence for the elastin gene. Thus, it is submitted that there is no motivation to combine Keating with Wydner et al. in the manner proposed by the Examiner.

In view of the above remarks, it is submitted that claims 3-4 are not rendered obvious by the cited prior art. Withdrawal of this rejection is requested.

The Examiner has rejected claims 5, 9 and 10 under 35 U.S.C. §103(a) as being obvious over Reitamo et al. (*Biochem J* 302:331-333, 1994) in view of Keating, in view of Wydner et al. It is submitted that the Examiner is in error in this rejection.

The Examiner cites Reitamo et al. for its teaching of transgenic mice containing a construct comprising a human elastin promoter and the chloramphenicol acetyltransferase reporter gene. These mice were injected with interleukin-10 to determine its effects on the elastin promoter. IL-10 was seen to upregulate the elastin promoter. The Examiner contends that it would have been obvious to substitute the WS patient of Keating or the mouse cells having only one functional elastin gene of Keating/Wydner et al. for the transgenic mouse of Reitamo et al., to screen for drugs or compounds useful in treating SVAS, hypertension or atherosclerosis.

As previously described, there is no motivation or suggestion in either Keating or Wydner et al. to make a transgenic mouse having a knockout of the elastin gene. In addition, since William's syndrome is known to involve a larger deletion than the elastin gene, as taught by

Keating, it is submitted that there would be no motivation to use a patient with William's syndrome to test for drugs which may be useful for treating SVAS, since other factors are involved. Furthermore, Reitamo et al. was interested in determining the effect of a cytokine, specifically IL-10, on the elastin promoter and not on the genetic basis of SVAS. There is no suggestion in Reitamo et al. to detect effect of the cytokine in a human or mouse model for SVAS. In the absence of such a suggestion in Reitamo et al., it is submitted that there is no motivation to combine Reitamo et al. with Keating and Wydner et al. to identify drugs which would be candidates for treating SVAS.

In view of the above remarks, it is submitted that claims 5, 9 an 10 are not rendered obvious by the cited prior art. Withdrawal of this rejection is requested.

In view of the amendments and above arguments, it is submitted that the present claims satisfy the provisions of the patent statutes and are patentable over the prior art. Reconsideration of this application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned to expedite allowance of this application.

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